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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,126	11/29/2001	Judith Aronhime	1662/50308	3388

26646 7590 06/03/2005

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EXAMINER	
POWERS, FIONA	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 06/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,126	ARONHIME ET AL.	
	Examiner	Art Unit	
	Fiona T. Powers	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/22/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *147-166,185,186 and 188* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *147-166* is/are allowed.

6)☒ Claim(s) *185,186 and 188* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/21/05, 5/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Receipt is acknowledged of the information disclosure statements filed April 21, 2005 and May 13, 2005, which have been entered in the file.

The indicated allowablility of claims 185, 186 and 188 is withdrawn due the to new rejection which follows.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 185, 186 and 188 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph are as follows:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of skill in the art.

See In re Wands, 8 USPQ2d 1400.

The nature of the invention is pharmaceutical compositions comprising crystalline forms of atorvastatin hemi-calcium and solvates thereof and methods of reducing low density lipoprotein particle concentration in the blood stream of a patient by administering the crystalline atorvastatin hemi-calcium or a solvate thereof.

The state of the prior art is that it is known that many compounds exist in more than one crystalline form (polymorphs). Polymorphs exist in more stable and less stable (metastable) forms. The preparation of pharmaceutical compositions requires creating solutions, milling, adding diluents, excipients, surfactants, etc. Drug companies must monitor the polymorph in the drug product to ensure that it persists during manufacture (Rouhi, Chemical and Engineering News, February 24, 2003, page 34). It is also the state of the prior art that an acceptable carrier for a pharmaceutical formulation can be water. Dissolving a specific crystalline form in water, creating an aqueous solution, would put the compound in its free form and

not in a crystalline form with a specific X-ray diffraction pattern.

The predictability or lack thereof in the art is that a metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern and also that a solution prepared from a specific crystalline form and water would contain the free form of the compound.

The only direction or guidance present in the instant specification is process for preparation of crystalline atorvastatin hemi-calcium. The specification fails to provide the steps of ensuring that the pharmaceutical compositions will maintain the specific forms as found in the specification and will not resort back to the free form or the most thermodynamically stable form of the compound and that the specific crystalline forms are given during the methods of treatment.

The breadth of the claims is pharmaceutical compositions comprising crystalline forms of atorvastatin hemi-calcium and solvates thereof and methods of reducing low density lipoprotein particle concentration in the blood stream of a patient by administering the crystalline atorvastatin hemi-calcium or a solvate thereof.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would be unable to maintain a specific metastable crystalline form upon preparation into a pharmaceutical composition which may require milling or the formation of a solution. Also, one of ordinary skill in the art would be unable to obtain a specific metastable crystalline form for the methods of treatment claimed.

While the level of skill in the art is high, one of ordinary skill in the art would be unable to maintain a specific metastable crystalline form upon the preparation of a pharmaceutical composition without direction and guidance that is not found in the instant specification. Of skill in the art would expect the pharmaceutical composition to contain the free form of the compound or the most thermodynamically stable form of the compound. Thus, the specification fails to provide sufficient support for pharmaceutical compositions comprising crystalline forms of atorvastatin hemi-calcium and solvates thereof and methods of reducing low density lipoprotein particle concentration in the blood stream of a patient by administering the crystalline atorvastatin hemi-calcium or a solvate thereof.

Action on applicants Request for Interference is postponed due to the new rejection given above.

Claims 147-166 are allowed.

The references made of record and not relied upon show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fiona T. Powers whose telephone number is 571-272-0702. The examiner can normally be reached on Monday - Friday 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fiona T. Powers
Fiona T. Powers
Primary Examiner
Art Unit 1626

ftp
May 31, 2005